REMARKS

Claims 1 and 3-54 were pending in this application. Claims 38-43 are canceled herein. Thus, after entry of this amendment, **claims 1, 3-37 and 44-54 will be pending**.

REJECTION UNDER 35 U.S.C. §103

Claims 1-17, 28, 30, 32, 34, 36 and 44-54 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Yasui *et al.* (*Southeast Asian J. Trop. Med. Public Health 21(4)*:663-669, 1990) in view of Kochel *et al.* (U.S. Patent No. 6,455,509), Ivy *et al.* (U.S. Patent No. 6,136,561), Phillpotts *et al.* (*Arch. Virol. 141*:743-749, 1996) and Kozak (*J. Mol. Biol. 196*:947-950, 1987) for the reasons of record. Briefly, the Office alleges it would have been obvious to one of ordinary skill in the art to prepare an expression cassette encoding the prM signal sequence and a flavivirus antigen as taught by Yasui *et al.* and to replace the antigen with immunogenic sequences from other flaviviruses as suggested by Kochel *et al.* and Ivy *et al.* The Office further states that Phillpotts *et al.* and Kozak provide the motivation to include the CMV-IE promoter and a ribosomal translational initiation sequence, respectively. Applicant traverses this rejection.

Applicant maintains that the cited references do not teach each and every element of the pending claims, and that one of ordinary skill in the art would have no reasonable expectation of success in view of the teachings of the cited references (see arguments presented in the Amendment and Response filed December 11, 2007). In addition, Applicant submits that the claimed nucleic acid molecules comprising transcriptional units encoding (i) a JEV signal sequence and (ii) an immunogenic antigen from another flavivirus or a chimeric flavivirus antigen, exhibit unexpectedly superior results over the results that one of ordinary skill in the art would expect based on the teachings of the cited references. In support of this argument, a Declaration under 37 C.F.R. §1.132 by the inventor of the application, Dr. Gwong-Jen J. Chang, is submitted herewith.

As discussed in detail in the Declaration, even a single inoculation with the claimed transcriptional units encoding a JEV signal sequence and an antigen from another flavivirus, or a chimeric flavivirus antigen, provides 100% protective immunity from lethal virus challenge, elicits significant neutralizing antibody titer, and provides passive protection by maternal

antibody. In particular, the specification describes pCBWN, a plasmid encoding a JEV signal sequence and the prM/E proteins from West Nile virus. A single dose of pCBWN led to the production of neutralizing antibodies and conferred complete protection to mice and horses against West Nile virus challenge (see Example 11 beginning on page 53 of the specification).

In addition, the specification teaches two dengue virus constructs, pCD9D2-1J-4-3 and pCB8D2-2J-2-9-1, in which the transcriptional units encode a JEV signal sequence, the prM protein from dengue virus and a chimeric E protein having sequences from both JEV (10% or 20%) and dengue virus (90% or 80%). Example 20 (beginning on page 65 of the specification) and the Chang *et al.* manuscript (submitted as Exhibit B) teach that a single inoculation of mice with either pCD9D2-1J-4-3 or pCB8D2-2J-2-9-1 resulted in 50% seroconversion or 100% seroconversion, respectively, within three weeks of immunization. In addition, a single dose of pCB8D2-2J-2-9-1 in female mice confers passive protection by maternal antibody to suckling pups. In addition, suckling pups of vaccinated mice survived challenge with a wild-type strain of dengue virus (see page 175 of Chang *et al.*).

None of the cited publications, or any references available in the prior art, teach a JEV signal sequence in combination with a flavivirus antigen from another flavivirus or a chimeric flavivirus antigen as claimed herein. Although it was known that signal sequences were important for efficient production of antigenic protein, one of skill in the art, given the teachings of the cited references, would not have been able to predict that the claimed transcriptional units would be capable of producing an immunogenic flavivirus antigen, particularly an immunogenic antigen capable of eliciting 100% protection from lethal virus challenge.

For at least the reasons stated above and in the Declaration, Applicant submits the claimed transcriptional units exhibit unexpectedly superior results over the combination of references cited by the Office. Accordingly, Applicant requests withdrawal of this rejection under 35 U.S.C. §103(a).

DOUBLE PATENTING

Claims 1, 3, 8-10, 13-17, 28, 32, 34, 36 and 44 are rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 7,227,011.

Applicant submits herewith a terminal disclaimer that disclaims the terminal portion of any patent granted in this application that would extend beyond the expiration date of U.S. Patent No. 7,227,011. Applicant submits that the submission of this terminal disclaimer obviates the rejection.

CONCLUDING STATEMENT

Applicant believes that the foregoing comprises a full and complete response to the Office action of record. Withdrawal of the pending rejections and allowance of the claims is respectfully requested. If the Examiner believes that there are any remaining issues in the case that could be resolved by a telephonic interview, the Examiner is encouraged to contact the representative for Applicant listed below to discuss any outstanding matters.

Respectfully submitted,

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